

Alterations in neurodevelopment and brain damage in neonates

Alterações no neurodesenvolvimento e danos cerebrais em neonatos

Alteraciones en el neurodesarrollo y daño cerebral en los neonatos

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ABSTRACT

Background: During fetal and neonatal development, the fetus's brain is in a critical growth development phase, making it susceptible to alterations that affect its correct functioning. These alterations occur more frequently in preterm neonates or in those whose mothers have presented a pathology during their gestation period or their age. **Objective:** Search for information about alterations in neurodevelopment and brain damage in neonates. **Methodology:** The research was conducted through a scientific bibliographic review answering the research question; databases such as Google Academic, Scielo, Dialnet, Scopus, and Pubmed were used to collect information. **Results:** 15 investigations were obtained as results, and after applying the different filters, only 3 met the information required for this investigation and were updated. **Discussion:** These alterations occur in the first instance due to prematurity, followed by the age of the mother and pathologies that can occur during pregnancy, being a problem for which neonates are referred to the intensive care unit. **Conclusion:** Early detection of alterations that may occur in neonates is of vital importance since when this does not happen in the neonate, it can cause disabilities throughout their life, such as cerebral palsy and even death..

Keywords: Neurodevelopmental alterations, neonates, brain damage, prematurity.

RESUMO

Contexto: Durante a fase de desenvolvimento fetal e neonatal, o cérebro do feto encontra-se numa fase crítica de crescimento-desenvolvimento, razão pela qual está suscetível a alterações que afetam o seu correto funcionamento. Estas alterações ocorrem com mais frequência nos neonatos prematuros ou prematuros. naqueles em que suas mães apresentaram alguma patologia durante a gestação ou na idade. **Objetivo:** Buscar informações sobre alterações no neurodesenvolvimento e danos cerebrais em neonatos. **Metodologia:** A pesquisa foi realizada por meio de revisão bibliográfica científica respondendo à questão de pesquisa foram utilizadas bases de dados como: Google Acadêmico, Scielo, Dialnet, Scopus, Pubmed; Resultados: obtiveram-se como resultados 15 investigações e após a aplicação dos diferentes filtros, apenas 3 atendiam às informações exigidas para esta investigação e que foram atualizadas. **Discussão:** Essas alterações ocorrem em primeiro lugar devido à prematuridade, seguida pela idade da mãe e patologias que podem ocorrer durante a gravidez, sendo um problema pelo qual os neonatos são encaminhados para a unidade de terapia intensiva. **Conclusão:** A detecção precoce de alterações que possam ocorrer no neonato é de vital importância, pois quando isso não acontece no neonato pode causar incapacidades ao longo da vida como paralisia cerebral e até morte.

Palavras-chave: Alterações do neurodesenvolvimento, neonatos, danos cerebrais, prematuridade.

RESUMEN

Antecedentes: Durante la etapa de desarrollo fetal y neonatal el cerebro del feto se encuentra en una fase crítica de crecimiento-desarrollo por lo que se encuentra susceptible a sufrir alteraciones que afectan al correcto funcionamiento del mismo, se presenta con mayor frecuencia estas alteraciones en los neonatos pretérmino o en aquellos donde sus madres hayan presentado una patología durante su periodo de gestación o la edad de la misma. **Objetivo:** Buscar información acerca de las alteraciones en el neurodesarrollo y daño cerebral en los neonatos. **Metodología:** La investigación se realizó mediante una revisión bibliográfica científica dando respuesta a la pregunta de investigación, para la recolección de información se utilizaron bases de datos como: Google Académico, Scielo, Dialnet, Scopus, Pubmed. **Resultados:** Se consiguieron como resultados 15 investigaciones y luego de la aplicación de los distintos filtros únicamente 3 cumplieron con información que se requería para esta investigación y que se encontraban actualizadas. **Discusión:** Estas alteraciones ocurren en primera instancia por la prematuridad, seguido de la edad de la madre y de patologías que se pueden presentar durante la gestación siendo una problemática por la cual los neonatos son derivados a la unidad de cuidados intensivos. **Conclusión:** La detección temprana de alteraciones que se pueden presentar en los neonatos son de vital importancia ya que cuando esto no sucede en el neonato puede provocar discapacidades a lo largo de su vida como la parálisis cerebral e inclusive la muerte.

Palabras clave: Alteraciones del neurodesarrollo, neonatos, daño cerebral, prematuridad.

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Early detection of neurodevelopmental alterations in neonates, particularly those born preterm or to mothers with pregnancy complications, is crucial to prevent long-term disabilities such as cerebral palsy. This article brings insights from the specialized literature that can guide policies and new studies related to neurodevelopment in neonates.

Originality/value:

The analytical synthesis presented addresses a very relevant and scarce topic in Latin American and developing country literature.

INTRODUCTION

The brain of a child is a structure that is in formation, therefore, it goes through several phases where cells create neuronal connections and all structures from the embryonic period with the aim of achieving their function, as well as their differentiation. During this stage of fetal and neonatal development, the brain of the fetus is in a critical period of growth-development, where it is vulnerable to suffering alterations that can cause neurologically based disorders, affecting its proper functioning (Alonso, 2023).

These alterations occasionally show up in structural lesions, although there is a possibility that they also occur due to a deficiency in the maturation of fibers that alter connectivity and, as a result, inadequate integration in neuronal communication (Kim, 2022). The bases of neurodevelopment come from adequate care, early learning, nutritional status and the prevention of diseases. When these bases are not well founded, there are alterations in neurodevelopment that cause deviations in brain function, for this reason The gestation period and the first 5 years of a child's life are essential for the well-being of physical, emotional, cognitive, psychological and social development that will be reflected throughout their life. (Alonso, 2023; Kim, 2022).

There are prenatal and perinatal risk factors that are related to the mother's condition and are associated with the existence of neurodevelopmental disorders, among them we have: maternal age at the time of pregnancy (mother under 18 years of age and mother aged over 35 years), substance consumption, nutritional factors, presence of infectious and contagious pathologies and accidents during embryonic development (Kim, 2022; Lepe, 2023).

Prematurity is the main cause of perinatal morbidity, which causes alterations in neurodevelopment and brain damage in neonates. Each year, approximately 15 million premature babies are born in the world, which is why it is necessary for the personnel who work in the neonatal intensive care (NICU) has expertise in managing patients (Barra, 2021; Cubillos, 2022; López, 2022; Pérez, 2024). In Latin America, the pathologies that occur most frequently during pregnancy are hypertensive disorders 25%, gestational diabetes 16% leading to preterm births in 25-43% of cases. Intrauterine infections, prematurity and neonatal asphyxia in 23% are related to neonatal alterations, in addition, these alterations that occur before and during birth represent 20% and are related to preterm births and low birth weight, resulting in alterations. of neurodevelopment where 13-24% present neurological disorders and 6-13% intellectual deficit. (Lepe, 2023; Barra, 2021; Millar, 2018; Salmón, 2024)

Likewise, the development of a brain injury in the premature newborn can occur due to different factors, among which we find perinatal asphyxia, infection, inflammation, chronic hypoxia and exposure to treatments that include mechanical ventilation and corticosteroids. Treatment is currently limited, the use of magnesium sulfate reduces in a small but important way the risk of cerebral palsy and gross motor dysfunction during early childhood, but its result in a combination of death or disability has not been proven to be effective. (Yates, 2021; Bachnas, 2021; Keir, 2022; Shepherd, 2024) On the other hand, preclinical studies emphasize several competent neuroprotective treatments, such as therapeutic hypothermia, melatonin, umbilical cord blood and vitamin D supplements, which help to reduce brain damage in premature neonates. (Yates, 2021 ; Wang, 2023; Xie, 2023; Razak 2023; Segler 2021)

Among the brain lesions in premature infants we find lesions of the white matter (WS), generally associated with neuronal and axonal alterations in the cerebral cortex and other areas of gray matter. SB injury also includes periventricular leukomalacia, which is a type of brain injury that affects premature babies. This condition involves the death of small areas of brain tissue around fluid-filled areas, called ventricles, as a result of this. holes are generated in the brain due to the damage caused. (Vinces, 2022; Schneider, 2019)

The incidence of severe hemorrhage, together with periventricular leukomalacia, constitutes the most serious threats to the brain of premature babies, being associated with greater morbidity and mortality and an adverse neurological prognosis. We classify intraventricular hemorrhage according to a brain ultrasound, leading to a classification of different grades (Grade I, Grade II, Grade III) according to the percentage of hemorrhage present at the time of performing an ultrasound. (Vinces, 2022; Pascal, 2023) Periventricular leukomalacia (PVL) is a type of brain injury, where "leuco" refers to the white matter of the brain, and "periventricular" refers to the area around the ventricles. An important cause of this condition is changes in blood flow around the ventricles of the brain. This is a very fragile area, therefore, it is very prone to injury, especially before 32 weeks of gestation. (Vinces, 2022; Valer, 2023; Perrone 2023)

Furthermore, ischemic lesions and hemorrhages in premature newborns are frequent complications in NICUs, periventricular leukomalacia and germinal matrix hemorrhage are two conditions that occur more frequently in premature newborns, thus becoming the main risk factors. associated with the development of cerebral palsy. (Vinces, 2022; Valer, 2023) Among the different risk factors and their incidence in the main types of brain injuries in premature infants, there are:

Lack of maturation with corticosteroids: The lack of administration or the incorrect dose of corticosteroids to the

mother during pregnancy can cause a lack of maturation of the fetus.

Severe depression: A 5-minute Apgar score of less than 6 points, or the need for endotracheal intubation at birth, are usually signs of severe depression.

Neonatal Sepsis: A clinical neonatal infection, confirmed by a blood culture, performed at any time during the hospitalization of the premature newborn. (Zarate, 2023)

Pneumothorax: An intrapleural air leak, with or without underwater pleural drainage.

Apnea: Presents as a lack of respiratory stimulation for 20 seconds or more, with or without oxygen desaturation, and with or without the need to administer xanthines.

Also a common condition in premature infants is focal necrosis of the cerebral white matter, accompanied by a diffuse gliosis reaction and activation of microglia in the affected area, this produces alterations in the functions of their oligodendroglial progenitors and in myelination, which can cause neurocognitive dysfunction. Likewise, this event may reflect damage to the gray matter of the brain, particularly in the thalamus, globus pallidus, hippocampus and dentate nucleus of the brain. These results indicate the severity of the disease and the need for a better understanding of the processes involved in the development of new, more effective therapies. (Vinces, 2022; Cerisola, 2019).

METHODOLOGY

The approach to be used will be the Systematic Review (S.R.), a research method that follows a thorough and clear process to identify, evaluate and summarize the available evidence related to a specific research question on a given topic. This process will be carried out using the PRISMA method to collect and organize data in a way that guarantees obtaining high-quality information (Linares-Espinós et al., 2018).

The criteria applied to select the articles are described below:

Inclusion criteria:

- Documents that contain titles with the terms Neurodevelopmental disorders, neonates, brain damage, prematurity.
- Agree with the search equation "Neurodevelopmental alterations AND neonates AND brain damage".
- Free access articles.
- Articles in English and Spanish languages.
- Articles that have been published between 2020 and 2024.
- Research with a methodological process and criteria that guarantee its rigor.

Exclusion criteria:

- Documents that are in languages that are difficult to translate.
- Articles without academic relevance and scientific verification.
- Documents not related to the topic.
- Repeated investigations

Search engines:

- Academic google, Pubmed, Elsevier, Scielo

Keywords were used as the main search strategy, along with filters that limit the selection of articles according to their year of publication, prioritizing the most recent ones. The keywords used are specified below.

Table 1. Literature search strategies.

Key terms	(Neurodevelopmental alterations) AND (neonates) AND (brain damage)
Language	English, Spanish
Boolean operators	AND, OR, NOT
Year of publication	Last 5 years, 2020- 2024
Main search sources	Academic Google, Pubmed, Elsevier, Scielo

Note. Prepared by the authors

Likewise, searches were carried out using different variables or search equations related to the keywords used.

Table 2. Main variables and modifications operated.

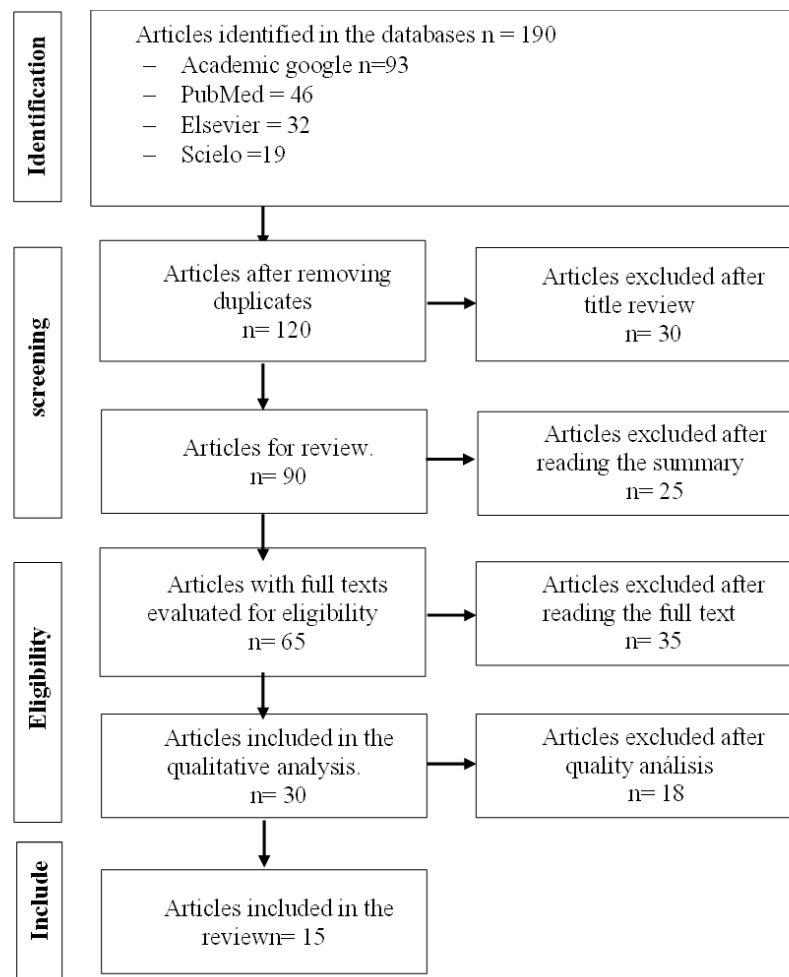
Main variables	Modification and implication of variables
Neurodevelopmental disorders	Congenital malformations in neonates
Brain damage	Brain alteration in neonates

Note. Prepared by the authors

The study selection process is based on the following criteria:

1. Initial reading of the research titles to determine their relevance to the objectives of the study.
2. Subsequently, the summaries of the documents are read, which allows us to delve deeper into the information of the articles and exclude those that are repeated or that do not meet the research inclusion criteria.
3. Finally, a complete and intensive reading of the articles selected for inclusion in the research is carried out. This step ensures a comprehensive understanding of the findings and contribution of each study to the body of knowledge in the area of interest.

Figure 1. Prism Diagram



Note. Prepared by the authors

After identifying the publications to be used, data were extracted, which were established through tables where the following indicators were proposed to classify the articles: title of the publication, author/s, year of publication/country, design of the study, results and analysis.

RESULTS AND DISCUSSION

Table 1. List of extracted data

Article title	Author/s	Year/Country	Study design	Results	Analysis
Characteristics of prematurity and neurodevelopmental alterations	Lepe Grajeda, JR, Paz Sandoval, AC, Panseits Rojas, BK & Sitavi Semeyá, ME	2023/Guatemala	Descriptive cross-sectional study with an analytical approach.	In this article it was shown that young first-time mothers under 18 years of age and older first-time mothers over 35 years of age have a high percentage of risk of premature birth, which could influence neurodevelopmental alterations in the child. Furthermore, if there is a greater degree of prematurity, the risk of neurodevelopmental disorders occurring is greater.	The research characterizes the risk factors in prematurity, as well as its possible alterations, so prematurity can influence neurodevelopment and the gestational age of the child at birth is a significant factor in determining the risk of developing neurodevelopmental disorders.
Perinatal risk factors and evolution of neurodevelopment until the first year of age	Abreu Díaz, L, Morilla Guzmán, A, Parada Marín, Y, Tamayo Pérez, V, Cabrerías Benites, E, and Rodríguez Cortina, D.	2021/Cuba	Descriptive, retrospective and longitudinal observational study.	In this article, perinatal risk factors for alterations in neurodevelopment were found where the male sex was predominant 68.4%, in addition to metabolic disorders 13.5% and perinatal asphyxia 11.2% that were related to neurodevelopmental alterations.	Perinatal risk factors that are related to alterations in neurodevelopment were male sex, low birth weight, prematurity, Apgar score at five minutes, sepsis, metabolic disorders, perinatal asphyxia and seizures. In addition, children with neurodevelopmental disorders may have improvement at one year of age due to medical and environmental interventions.
Risk of brain damage in premature infants under 34 weeks exposed to histological chorioamnionitis, Lima, Peru	Guillén, N., Llerena, C., Samalvides, S., Vila, J., Juárez, T., Cáceres, J., and Guillén-Pinto, D.	2020/ Peru	Retrospective and descriptive study.	In this article it was found that histological chorioamnionitis (CAH) is a risk factor for developing brain lesions in premature infants under 34 weeks.	Histological chorioamnionitis has fatal effects at different ages of preterm infants under 34 weeks, including the risk of producing or contributing to early and late brain lesions. Finally, this study highlights the importance of histological examination of the placenta and its relationship with neurological and ultrasound monitoring.
Prematurity: epidemiology, causes and consequences, first place in mortality and disability.	Matos, LJ, Reyes, K, López Navarrete, G., Reyes, M., Aguilar, E., Pérez, O., Reyes, U., López Cruz, G., Flores, B., Quero Hernández, A., and Quero Estrada, A.	2020/ Mexico	Descriptive and retrospective study.	In this article, it was found that prematurity is the first cause of mortality and is also responsible for a large number of disabilities and adverse events, including neurodevelopmental, physiological, respiratory, metabolic, and immunological complications, among others.	Prematurity is a serious public health problem due to the great morbidity and mortality it causes, in addition to the high economic and social costs caused by its care, which is why it is essential to address this problem through the implementation of policies and comprehensive action plans to minimize health inequality, especially between women and neonates.
Prevalence of alterations in motor neurodevelopment in premature children without a diagnosis of cerebral palsy.	Millar, PA, Navarro, J.-J., Martella, D. and Gallardo, CP	2018/ Chile	Cross-sectional descriptive or prevalence study.	In this article it was shown that 69.56% of children with a history of extreme prematurity or very premature children had mild psychomotor developmental delay.	Prematurity is associated with alterations in motor neurodevelopment, especially in children with extreme prematurity and very premature. Also, it is important to consider these alterations in the diagnosis and treatment of premature children to guarantee optimal development.
Monitoring of neurodevelopment in late preterm newborns up to two years of age.	Torres López, A., Morilla Guzmán, A., Sánchez Villavicencio, C., Rosabal Vior, L., Santana Noda, M., and Argüelles Matos, A.	2019/ Cuba	Retrospective, observational, analytical and longitudinal study.	In this research, a higher incidence of neurodevelopmental alterations was observed in late preterm newborns at 6 months 18.8%, at 1 year 8.7% and at 2 years 7.7%, in addition this group had a greater need for mechanical ventilation and the use of anticonvulsant drugs, with a predominance of the male sex and birth by cesarean section to present these neurodevelopmental alterations.	Birth by cesarean section stands out in late preterm newborns; these neonates have a greater need for mechanical ventilation and resuscitation at the time of birth, which is why this group has greater neurodevelopmental impairment and a greater risk of hearing loss.
Prevalence of alterations in neurodevelopment in children from a rural population of Oaxaca evaluated using the Child Development Assessment test.	Alonso López, N., Hernández Valle, V., Pedroza Vargas, ME, & García Medina, NE.	2023/ Mexico	Descriptive, cross-sectional and prospective study	In the article, a prevalence of alterations in neurodevelopment was found, predominantly in the male sex, with language as the area of greatest affection with 29%, neurological conditions only occurred in 2% of the total participants, in addition, the factor of The risk that had the highest prevalence is urinary infections in mothers with 56%.	Alterations in neurodevelopment are more prevalent in rural communities with a percentage of 30% due to the social risk factors that children experience, thus having difficult access to medical care, unstimulating environments and poor nutrition. The contact of health professionals with pediatric patients early is important for the detection of alterations in neurodevelopment, allowing timely diagnosis and treatment.
Neonatology. Brain injuries in premature babies.	Vinces Menéndez, C., Calderón, VDR, Auquilla, RET, and Moreno, MPV	2022/ Ecuador	Systematic review and meta-analysis of controlled clinical trials.	Within this research it was found that brain lesions are one of the main adverse consequences of premature birth, among the lesions that are associated are white matter (WM) lesions, mainly periventricular leukomalacia (PVL) and intracranial hemorrhages (HIC), whose risk factors are related to the development of cerebral palsy.	These lesions can be avoided with continuous prenatal monitoring since they help identify anomalies present from the stage of embryonic development. Even though the survival of the premature neonate has increased over time, prematurity is related to the development of brain lesions, whose manifestation occurs from the first minutes of life until the consequences are evident in middle age.
Feasibility of Umbilical Cord Blood Collection in Neonates at Risk of Brain Damage—A Step Toward Autologous Cell Therapy for a High-risk Population."	Segler, A., Braun, T., Fischer, HS, Dukatz, R., Weiss, CR, Schwicker, A., Jäger, C., Bührer, C., & Henrich, W.	2021/ United States	Observational and retrospective study.	In this article, through the collection of umbilical blood, it was shown that 10.7% of the included neonates developed brain lesions.	Umbilical blood collection in neonates at risk of brain damage is feasible with a multidisciplinary approach and intensive follow-up, as the quality and quantity of cells obtained are critical for potential treatment in preterm neonates.
Effect of perinatal asphyxia and body hypothermia on auditory evoked potentials and development in the first two years of life.	Soler Limón, KM., Romero Esquiliano, G., Romero Gutiérrez, PV., Orozco A., Calderón, C., and Rivera, R.	2022/ Mexico	Prospective, descriptive and longitudinal study.	With the use of body hypothermia therapy as a neuroprotector in the first 72 hours, it has been possible to improve the survival of neonates, as well as the neurodevelopmental results in cases with moderate to severe Hypoxic-Ischemic Encephalopathy (HIE). PEATC values were similar to those observed in healthy children and were significantly correlated with development at both ages.	The PEATC showed a relationship with subsequent development; The characterization of normality/alteration that we proposed allowed us to show the PEATC as an indicator of risk for development, even before frank damage to the auditory pathway.
Safety and effectiveness of therapeutic hypothermia in neonates with mild hypoxic-ischemic encephalopathy.	Wang, Z., Zhang, D., Zhang, P., Zhou, W., Hu, L., Wang, L., & Cheng, G.	2023/ China	Retrospective study	In this article it was shown that therapeutic hypothermia reduced the incidence of brain injuries in neonates with mild hypoxic-ischemic encephalopathy.	Therapeutic hypothermia is an effective and safe therapy to reduce the incidence of brain injuries in neonates with mild hypoxic-ischemic encephalopathy.
Chorioamnionitis and risk of long-term neurodevelopmental disorders in offspring: a population-based cohort study.	Tsamantioti, E., Lisonkova, S., Muraca, G., Örtqvist, A.K., & Razaz, N.	2022/ Sweden	Retrospective population-based cohort study	In this article it was found that 5770 offspring were exposed to chorioamnionitis during the pregnancy stage. During the follow-up time of the study, there were 0.21% cases of cerebral palsy in addition to 0.80% cases of epilepsy, continuing with 2.27% cases of autism and 5.12% cases of attention deficit hyperactivity disorder, after adjusting for potential confounders, exposure to chorioamnionitis increased the risk ratios for cerebral palsy.	Chorioamnionitis increases the risk of neurodevelopmental disorders mainly cerebral palsy, autism, attention deficit hyperactivity disorders and intellectual disability, these associations were mainly mediated by premature birth, timely identification and appropriate interventions to treat infections during pregnancy since They have benefits focused on reducing the burden of neurological complications in children at the population level.
Histological chorioamnionitis and neurodevelopment in premature children under 34 weeks, Lima-Peru.	Vila, Judith, Guillén-Pinto, Daniel, Bellomo, Sicilia, and Guillén, Noelia.	2023/ Peru	Retrospective study	In this article, histological chorioamnionitis did not show influence on neurodevelopment in premature infants less than 34 weeks at 2 years of age, which means that it has no long-term effects.	Histological chorioamnionitis is not associated with long-term neurodevelopmental disorders in premature infants younger than 34 weeks. However, additional studies are recommended to evaluate the impact of chorioamnionitis on neurodevelopment.
Brain anatomopathological findings in neonates with congenital heart disease.	Carina-Kaiser, Ferial, Lorena-Hernández, Luis M., González-Cabello, Héctor J., Segura-Esquível, Amanda A., & Rodríguez-Velasco, Alicia.	2022/ Mexico	Retrospective and descriptive study	In this article, it was found that brain lesions in neonates with congenital heart disease are characterized by lesions of the white matter (WM), mainly periventricular leukomalacia (PVL) and intracranial hemorrhages (ICH), whose risk factors are associated with the development of cerebral palsy.	The total number of children with complex congenital heart diseases presented some degree of hypoxic-ischemic injury and 35% had some type of hemorrhage. There are various risk factors for neurological damage which are impossible to control in their entirety.
Neurodevelopment in very low weight newborns born in Matanzas in the period 2016-2018.	Robaina Castellanos, Gerardo Rogelio, Riesgo Rodríguez, Solangel de la Caridad, & Hernández Morales, Dariana.	2022/Cuba	Prospective observational study	This article showed that neurodevelopmental alterations in very low birth weight premature infants constitute up to 50% of childhood neurological abnormalities.	Neonatal seizures are a common sign of neurological dysfunction in very low birth weight newborns.

Note. Own elaboration with the research data (2023)

In the study carried out by Lepe, in relation to the factors that contribute to neurodevelopmental alterations in premature children and the incidence of the mother's age, the result is that 55.6% of mothers under 18 years of age and elderly mothers are. That is, those over 35 years of age are more likely to have a preterm birth, which as a consequence has a greater risk of neurodevelopmental alterations in the child. As well as, the pathologies that the mother presents during pregnancy are 85% risk factors for premature birth and those that are acquired during this stage with 15% are factors that influence the neurodevelopment of the premature child. (Lepe, 2023). Furthermore, in the study carried out by Abreu Diaz, perinatal risk factors for alterations in neurodevelopment were found where the male sex was predominant 68.4%, in addition to metabolic disorders 13.5% and perinatal asphyxia 11.2% that were related to alterations of the neurodevelopment. (Abreu, 2021)

Torres in his research indicates that there is a higher incidence of neurodevelopmental alterations in late preterm newborns at 6 months 18.8%, at 1 year 8.7% and at 2 years 7.7%, they also had a greater need for ventilation mechanics and the use of anticonvulsant drugs, predominating the male sex and birth by cesarean section to present these neurodevelopmental alterations, having a relationship with the research of Lepe and Abreu. (Torres, 2019). For his part, Alonso López, found a prevalence of alterations in neurodevelopment predominating in the male sex, with language being the area of greatest affectation with 29%, neurological conditions only occurred in 2% of the total participants, in addition, the risk factor that had the highest prevalence is urinary infections in mothers with 56%. (Alonso López, 2023). Guillén, in the results of his research, showed that histological chorioamnionitis (CAH) is a risk factor for developing brain lesions in premature babies under 34 weeks. (Guillén, 2020). On the other hand, Vila showed that CAH did not show influence on neurodevelopment at two years of age, which means that it does not have long-term effects. (Vila, 2023)

Vinces, in his research, found that brain lesions are one of the main adverse consequences of premature birth. Among the associated lesions are white matter (WM) lesions, mainly periventricular leukomalacia (PLV) and intracranial hemorrhages (ICH), whose risk factors are related to the development of cerebral palsy, agreeing with Carina's study. (Vinces, 2022; Carina, 2022). Also, for his part, Segler, through the collection of umbilical blood, showed that 10.7% of the neonates included in his study developed brain lesions. (Segler, 2021).

In the study carried out by Matos, it was found that prematurity is the first cause of mortality and is also responsible for a large number of disabilities and adverse events, including neurodevelopmental, physiological, respiratory, metabolic, and immunological complications, among others. (Matos, 2020). In his research, Millar showed that 69.56% of children with a history of extreme prematurity or very premature children had mild psychomotor developmental delay. (Millar, 2018). Also, Robaina Castellanos in her research found that neurodevelopmental alterations in very low birth weight premature babies constitute up to 50% of the neurological abnormalities of childhood.

Soler and Wang, in their research, mention that with the use of body hypothermia therapy as a neuroprotector in the first 72 hours, it has been possible to improve the survival of neonates, as well as the results in neurodevelopment in cases with Hypoxic-Ischemic Encephalopathy. (HIE) mild, moderate and severe. PEATC values were similar to those observed in healthy children and were significantly correlated with development at both ages. (Soler, 2022; Wang, 2023). Moreover, Tsamantioti, in his research with 5770 offspring who were exposed to chorioamnionitis during the pregnancy stage, during the follow-up time of the study, there were 0.21% cases of cerebral palsy in addition to 0.80% cases of epilepsy, continuing with 2.27% cases of autism and 5.12% cases of attention deficit hyperactivity disorder, after adjusting for potential confounders, exposure to chorioamnionitis increased the risk ratios for cerebral palsy.

The literature consistently indicates that prematurity, maternal age, and maternal health conditions are significant contributors to neurodevelopmental alterations and brain damage in neonates. There is a clear emphasis on the importance of early detection and intervention to reduce the long-term impact of these conditions, with particular attention to the effectiveness of therapeutic strategies like body hypothermia in improving outcomes for affected neonates. The findings emphasize the complex interaction of prenatal and perinatal factors in shaping neonatal brain development and highlight the constant need for targeted research and clinical strategies to address these challenges.

CONCLUSIONS

There are prenatal and perinatal risk factors that are related to the mother's condition and are linked to the existence of alterations in neurodevelopment, among them we have: prematurity, maternal age at the time of pregnancy, substance consumption, nutritional factors, presence of infectious and contagious pathologies, birth by cesarean section, evaluation of the low Apgar test at the fifth minute of birth, male sex, low birth weight, neonatal sepsis, systemic inflammatory response syndrome, hypocalcemia, hypoglycemia, neonatal asphyxia, seizures and accidents during embryonic development.

In addition, SB injury, including periventricular leukomalacia, affects premature babies, as it involves the death of fluid-filled ventricles, resulting in holes in the brain due to the damage caused. Thus we have that the neurodevelopmental

alterations that occur most in premature children are cognitive, linguistic, emotional and motor. Finally, based on all the arguments raised and supported in this article, it was determined that the early detection of alterations that may occur in neonates is of vital importance since when this does not happen in the neonate it can cause disabilities throughout life. your life such as cerebral palsy and even cause death.

Limitations and future research

Among the limitations of the study is that there is limited information about the topic of study in Ecuador, so the importance of expanding lines of research that help create protocols that support care in neonates with this pathology based on scientific evidence is emphasized. Future studies in Ecuador and other developing countries should focus on how socioeconomic factors, such as access to prenatal care and maternal education, influence the incidence and severity of neurodevelopmental alterations in neonates. Research also should explore the effectiveness of affordable, early intervention strategies for preventing neurodevelopmental damage in preterm neonates, particularly in under-resourced healthcare systems typical of developing nations.

REFERENCES

- Abreu Díaz, L., Morilla Guzmán, A., Parada Marín, Y., Tamayo Pérez, V., Cabrerías Benites, E., y Rodríguez Cortina, D. (2021). Factores de riesgo perinatales y evolución del neurodesarrollo hasta el primer año de edad. *Revista Cubana de Pediatría*, 93(4). http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S0034-75312021000400007&lng=es&tlng=es.
- Alonso López, N., Hernández Valle, V., Pedroza Vargas, ME, & García Medina, NE (2023). Prevalencia de alteraciones en el neurodesarrollo en niños de la población rural de Oaxaca evaluados mediante la prueba Evaluación de Desarrollo Infantil. *Revista de neurología*, 76(02), 41. <https://doi.org/10.33588/rn.7602.2022240>
- Barra C, L., Marín P, A., y Coó, S. (2021). Cuidados del desarrollo en recién nacidos prematuros: fundamentos y características principales. *Andes pediatria: revista chilena de pediatría*, 92(1), 131–137. <https://doi.org/10.32641/andespediatr.v92i1.2695>
- Bachnas, M. A., Akbar, M. I. A., Dachlan, E. G., & Dekker, G. (2021). The role of magnesium sulfate (MgSO₄) in fetal neuroprotection. *The journal of maternal-fetal & neonatal medicine: the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians*, 34(6), 966–978. <https://doi.org/10.1080/14767058.2019.1619688>
- Carina-Kaiser, Ferial, Lorenzo-Hernández, Luis M., González-Cabello, Héctor J., Segura-Esquivel, Amanda A., & Rodríguez-Velasco, Alicia. (2022). Hallazgos anatomopatológicos cerebrales en neonatos con cardiopatía congénita. *Gaceta médica de México*, 158(1), 24-31. Epub 25 de abril de 2022. <https://doi.org/10.24875/gmm.21000385>
- Cerisola, A., Baltar, F., Ferrán, C., y Turcatti, E. (2019). Mecanismos de lesión cerebral en niños prematuros. *Medicina (Buenos Aires)*, 79(Supl. 3), 10-14. http://www.scielo.org.ar/scielo.php?script=sci_arttext&pid=S0025-76802019000700004&lng=es&tlng=es.
- Cubillos-Bravo, R., & Avello-Sáez, D. (2022). Tecnologías de apoyo a la rehabilitación e inclusión. Recomendaciones para el abordaje de niñas, niños y adolescentes con trastornos del neurodesarrollo. *Revista médica Clínica Las Condes*, 33 (6), 604–614. <https://doi.org/10.1016/j.rmcl.2022.10.003>
- Guillén, N., Llerena, C., Samalvides, S., Vila, J., Juárez, T., Cáceres, J., y Guillén-Pinto, D. (2020). Riesgo de daño cerebral en prematuros menores de 34 semanas expuestos a corioamnionitis histológica, Lima, Perú. *Revista Peruana de Medicina Experimental y Salud Pública*, 37(2), 229-238. <https://dx.doi.org/10.17843/rpmesp.2020.372.4779>
- Keir, A. K., Shepherd, E., McIntyre, S., Rumbold, A., Groves, C., Crowther, C., & Callander, E. J. (2022). Antenatal magnesium sulfate to prevent cerebral palsy. *Archives of disease in childhood. Fetal and neonatal edition*, 107(2), 225–227. <https://doi.org/10.1136/archdischild-2021-321817>
- Kim, S. W., Youk, T., & Kim, J. (2022). Maternal and Neonatal Risk Factors Affecting the Occurrence of Neurodevelopmental Disorders: A Population-Based Nationwide Study. *Asia-Pacific journal of public health*, 34(2-3), 199–205. <https://doi.org/10.1177/10105395211066383>
- Lepe Grajeda, J. del R., Paz Sandoval, AC, Panseits Rojas, BK, y Sitaví Semyá, ME (2023). Características de la prematuridad y alteraciones del neurodesarrollo. *Revista Académica Sociedad del Conocimiento Cuzcaco*, 3(1), 197–205. <https://doi.org/10.46780/sociedadcuzcaco.v3i1.80>
- Linares-Espinós, E., Hernández, V., Domínguez-Escrib, J. L., Fernández-Pello, S., Hevia, V., Mayor, J., Padilla-Fernández, B., & Ribal, M. J. (2018). Metodología de una revisión sistemática. *Actas Urológicas Españolas*, 42(8), 499–506. <https://doi.org/10.1016/j.acuro.2018.01.010>
- López, I., & Förster, J. (2022). Trastornos del neurodesarrollo: dónde estamos hoy y hacia dónde nos dirigimos. *Revista médica Clínica Las Condes*, 33 (4), 367–378. <https://doi.org/10.1016/j.rmcl.2022.06.004>
- Matos, L.J., Reyes, K., López Navarrete, G., Reyes, M., Aguilar, E., Pérez, O., Reyes, U., López Cruz, G., Flores, B., Quero Hernández, A., y Quero Estrada, A. (2020). La prematuridad: epidemiología, causas y consecuencias, primer lugar de mortalidad y discapacidad. *Sal Jal*, 7(3), 179-186. <https://www.medigraphic.com/cgi-bin/new/resumenl.cgi?IDARTICULO=98553&idP=9291>
- Menéndez, C. V. V., Calderón, V. D. R., Auquilla, R. E. T., y Moreno, M. P. V. (2022). Neonatología. Lesiones cerebrales en prematuros. Análisis del comportamiento de las líneas de crédito a través de la corporación financiera nacional y su aporte al desarrollo de las PYMES en Guayaquil 2011-2015, 6(2), 470–477. [https://doi.org/10.26820/recimundo/6.\(2\).abr.2022.470-477](https://doi.org/10.26820/recimundo/6.(2).abr.2022.470-477)
- Millar, PA, Navarro, J.-J., Martella, D. y Gallardo, CP (2018). Prevalencia de alteraciones del neurodesarrollo motriz en niños prematuros sin diagnóstico de parálisis cerebral. *Fisioterapia (Madrid. Ed. impresa)*, 40 (6), 305–311. <https://doi.org/10.1016/j.ft.2018.10.001>
- Pascal, A., de Bruyn, N., Naulaers, G., Ortbis, E., Hanssen, B., Oostra, A., de Coen, K., Sannaert, M., Cloet, E., Casaer, A., D'Haese, J., Laroche, S., Jonckheere, A., Plaskie, K., van Mol, C., Bruneel, E., van Hoestenbergh, M. R., Samijn, B., Govaert, P., & Van den Broeck, C. (2023). The Impact of Intraventricular Hemorrhage and Periventricular Leukomalacia on Mortality and Neurodevelopmental Outcome in Very Preterm and Very Low Birthweight Infants: A Prospective Population-based Cohort Study. *The Journal of pediatrics*, 262, 113600. <https://doi.org/10.1016/j.jpeds.2023.113600>
- Perez, S., y Fernandez, A. (2024). Relaciones entre signos motores tempranos y evolución cognitiva posterior en niños prematuros: una revisión sistemática | Relaciones entre signos motores tempranos y la posterior evolución cognitiva en niños prematuros: una revisión sistemática. *Fisioterapia*. <https://www.sciencedirect.com/science/article/abs/pii/S0211563824000361>

- Perrone, S., Grassi, F., Caporilli, C., Boscarino, G., Carbone, G., Petrolini, C., Gambini, L. M., Di Peri, A., Moretti, S., Buonocore, G., & Esposito, S. M. R. (2023). Brain Damage in Preterm and Full-Term Neonates: Serum Biomarkers for the Early Diagnosis and Intervention. *Antioxidants* (Basel, Switzerland), 12(2), 309. <https://doi.org/10.3390/antiox12020309> <https://doi.org/10.1001/jamanetworkopen.2023.7473>
- Robaina Castellanos, Gerardo Rogelio, Riesgo Rodríguez, Solangel de la Caridad, & Hernández Morales, Dariana. (2022). Neurodesarrollo en recién nacidos de muy bajo peso nacidos en Matanzas en el periodo 2016-2018. *MediSur*, 20(3), 455-468. Epub 30 de junio de 2022. Recuperado en 13 de junio de 2024, de http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1727-897X2022000300455&lng=es&tlng=es.
- Razak, A., Patel, W., Durrani, N. U. R., & Pullattayil, A. K. (2023). Interventions to Reduce Severe Brain Injury Risk in Preterm Neonates: A Systematic Review and Meta-analysis. *JAMA network open*, 6(4), e237473.
- Salmon, F., Kayem, G., Maisonneuve, E., Foix-L'Hélias, L., Benhammou, V., Kaminski, M., Marchand-Martin, L., Kana, G., Subtil, D., Lorthe, E., Ancel, P.-Y., Letouzey, M., Boileau, P., Butin, M., Gras-Le Guen, C., Kuhn, P., Letouzey, M., Mitha, A., Torchin, H., y Charlier, C. (2024). Clinical chorioamnionitis and neurodevelopment at 5 years of age in children born preterm: The EPIPAGE-2 cohort study. *The Journal of Pediatrics*, 267(113921), 113921. <https://doi.org/10.1016/j.jpeds.2024.113921>
- Schneider, J., & Miller, S. P. (2019). Preterm brain Injury: White matter injury. *Handbook of clinical neurology*, 162, 155-172. <https://doi.org/10.1016/B978-0-444-64029-1.00007-2>
- Segler, A., Braun, T., Fischer, H. S., Dukatz, R., Weiss, C. R., Schwickert, A., Jäger, C., Bühner, C., & Henrich, W. (2021). Feasibility of Umbilical Cord Blood Collection in Neonates at Risk of Brain Damage-A Step Toward Autologous Cell Therapy for a High-risk Population. *Cell transplantation*, 30, 963689721992065. <https://doi.org/10.1177/0963689721992065>
- Shepherd, E. S., Goldsmith, S., Doyle, L. W., Middleton, P., Marret, S., Rouse, D. J., Pryde, P., Wolf, H. T., & Crowther, C. A. (2024). Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. *The Cochrane database of systematic reviews*, 5(5), CD004661. <https://doi.org/10.1002/14651858.CD004661.pub4>
- Soler Limón, KM., Romero Esquiliano, G., Romero Gutiérrez, PV., Orozco A., Calderón, C., y Rivera, R. (2022). Efecto de la asfisia perinatal e hipotermia corporal en los potenciales evocados auditivos y el desarrollo en los primeros dos años de vida. *Arco Neurocién*, 27(2):58-10. <https://www.medigraphic.com/cgi-bin/new/resumen.cgi?IDARTICULO=106569>
- Torres López, A., Morilla Guzmán, A., Sánchez Villavicencio, C., Rosabal Vior, L., Santana Noda, M., y Argüelles Matos, A. (2019). Seguimiento del neurodesarrollo en los recién nacidos pretérminos tardíos hasta los dos años de edad. *Revista Cubana de Pediatría*, 91(3). http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S0034-75312019000300007&lng=es&tlng=es.
- Tsamantioti, E., Lisonkova, S., Muraca, G., Örtqvist, A. K., & Razaz, N. (2022). Chorioamnionitis and risk of long-term neurodevelopmental disorders in offspring: a population-based cohort study. *American Journal of Obstetrics and Gynecology*, 227(2), 287.e1-287.e17. <https://pubmed.ncbi.nlm.nih.gov/35305960/>
- Valer, A., Maldonado, A., Jiménez, M., Jubero, A., Vera, N., y Souto C. (2023). Relación entre prematuridad y parálisis cerebral. *Revista Sanitaria de Investigación*. <https://revistasanitariadeinvestigacion.com/relacion-entre-prematuridad-y-paralisis-cerebral/>
- Vila, Judith, Guillén-Pinto, Daniel, Bellomo, Sicilia, y Guillén, Noelia. (2023). Corioamnionitis histológica y neurodesarrollo en niños prematuros menores de 34 semanas, Lima-Perú. *Acta Médica Peruana*, 40(2), 113-119. Epub 30 de junio de 2023. <https://dx.doi.org/10.35663/amp.2023.402.2576>
- Vinces Menéndez, C., Calderón, V. D. R., Auquilla, R. E. T., y Moreno, M. P. V. (2022). Neonatología. Lesiones cerebrales en prematuros. Análisis del comportamiento de las líneas de crédito a través de la corporación financiera nacional y su aporte al desarrollo de las PYMES en Guayaquil 2011-2015, 6(2), 470-477. [https://doi.org/10.26820/recimundo/6.\(2\).abr.2022.470-477](https://doi.org/10.26820/recimundo/6.(2).abr.2022.470-477)
- Wang, Z., Zhang, D., Zhang, P., Zhou, W., Hu, L., Wang, L., & Cheng, G. (2023). Safety and efficacy of therapeutic hypothermia in neonates with mild hypoxic-ischemic encephalopathy. *BMC pediatrics*, 23(1), 530. <https://doi.org/10.1186/s12887-023-04365-8>
- Xie, Y., Yang, Y., & Yuan, T. (2023). Brain Damage in the Preterm Infant: Clinical Aspects and Recent Progress in the Prevention and Treatment. *CNS & neurological disorders drug targets*, 22(1), 27-40. <https://doi.org/10.2174/1871527321666220223092905>
- Yates, N., Gunn, A. J., Bennet, L., Dhillon, S. K., & Davidson, J. O. (2021). Preventing Brain Injury in the Preterm Infant-Current Controversies and Potential Therapies. *International journal of molecular sciences*, 22(4), 1671. <https://doi.org/10.3390/ijms22041671>
- Zarate, M., Sáenz, C., Canella, R., Díaz, M., Josefina, D.A., y Solana, C. (2023). Prevalencia de sepsis neonatal confirmada microbiológicamente en una maternidad de la Ciudad Autónoma de Buenos Aires. *Archivos argentinos de pediatría*, 121(3), 8. <https://dx.doi.org/10.5546/aap.2022-02779>
- Zea-Vera, A., Turín, CG., Rueda, MS., Guillén-Pinto, D., Medina-Alva, P., Tori A,Rivas, M., Zerraga, J., Castañeda, A., Cam, L., y Ochoa, T. (2019). Hemorragia intraventricular y leucomalacia periventricular en neonatos de bajo peso al nacer en tres hospitales de Lima, Perú. *Rev Peru Med Exp Salud Publica*. 36(3):448-53. http://www.scielo.org.pe/scielo.php?script=sci_arttext&pid=S1726-46342019000300448

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A. theoretical and conceptual foundations and problematization:	20%	20%	20%	20%	20%
B. data research and statistical analysis:	20%	20%	20%	20%	20%
C. elaboration of figures and tables:	20%	20%	20%	20%	20%
D. drafting, reviewing and writing of the text:	20%	20%	20%	20%	20%
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